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# HYPERSENSITIVENESS AND ASTHMA, ESPECIALLY IN RELATION TO EMANATIONS FROM HORSES

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Some years ago I described<sup>1</sup> a case of marked sensitiveness to horse serum, the chief features of which may be restated here:

1. It concerns a physician, aged 30, who as far back as he can recall would begin to suffer from symptoms of hay-fever and asthma soon after coming in close contact with horses as in driving, going into a stable or circus. He could drive a comparatively short distance only, without symptoms appearing; he could smell whether the horse was nicely groomed or not; in streets where there was much dust mixed with horse droppings symptoms would come on quickly; sitting beside persons whose clothes smelt of horses might bring on asthma.

One aunt and a distant relative have asthma, and one uncle and a cousin have hay-fever, but none of his brothers, sisters or other relatives are affected as he is by horses.

In December, 1908, he was given 2 c c (1,000 units) of diphtheria antitoxin as he had been exposed to diphtheria, and within 5-10 minutes the eyes commenced to itch intensely, the nose to run, and coughing with dyspnea set in. The dyspnea grew worse rapidly, cyanosis developed, the pulse could hardly be counted, and he felt extremely weak. After about 2 hours the symptoms began to subside, and the next day he felt quite well again. A large area of redness with some edema developed about the point of injection.

After this acute intoxication, which was not unlike the anaphylactic shock of the sensitized guinea-pig, the patient could be near horses without any bad effects, but after about 4 months the old sensitiveness returned. About 5 c c of the serum of the patient was injected into the abdominal cavity of a guinea-pig without any ill effects; 48 hours later the animal received an injection of horse serum whereupon anaphylactic shock supervened. This experiment was repeated later with the same result, the guinea-pig now dying from the shock. Somewhat later an attack of asthma was traced to eating sausages containing horse meat as shown by the precipitin test. It was also found that putting a small amount of horse serum on a small scratch in the skin of the arm would be followed in from 2-10 minutes by a local swelling from 1.5-2 cm. in diameter due to edema; further that if a horse was stroked with a finger which was then applied to the conjunctiva an intense redness would appear in a few minutes. Dropping horse serum in the eye would also cause a brief redness. Exposure to other animals (cattle, sheep, dog, cat) was without effect; the odor of rabbits and guinea-pigs might provoke mild symptoms, and rabbit serum caused a reaction in the skin.

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<sup>1</sup>Norsk Magazin for Lægevidenskaben, 1909, 5 R., 7, p. 569.

Similar observations have been made by others, notably Gillette,<sup>2</sup> and I have had the chance to observe several cases of "horse asthma," which I shall report in brief.

2. A woman, aged 36, had occasional attacks of asthma in childhood and when she became 10 years old it was noticed that they would come on when driving, going into stables and in streets where there was much traffic; when still older, asthma would come on in the winter also, and since reaching her 30th year the attacks have been worse. She has no hay-fever, but a sister has, and an uncle had asthma in his old age. By staying 30 minutes in a stable with horses, itching and running of the eyes would set in, also running from the nose, cough and typical asthma. Horse serum gave a well marked skin reaction and she also developed conjunctival redness on touching the conjunctiva with a finger with which a horse had been touched.

3. A woman, aged 24, always acquired redness of the eyes, nasal irritation, and asthma when driving with horses for some time. No hay-fever, but a sister has, and an aunt has bronchial asthma. After remaining in a stable for 10 minutes the nose began to flow, the conjunctivae became irritated, the lips blue, and there was some coughing with râles over the lungs; complete recovery in 3 hours. Horse serum gave a marked skin reaction (edema), which disappeared in 1½ hours; touching the eye with a finger which had just touched a horse caused marked redness, increased flow of tears, and sneezing. The only other animals, contact with which would produce any of these symptoms, were the rabbit and the guinea-pig.

4. A man, aged 45, often had asthma since childhood, and since his 7th year the attacks would come on when going into stables and on driving; attacks would also come on without coming into close contact with horses, but only in the city, never in the country. Several members of his family were asthmatics or had hay-fever. Since his 14th year he has been a sea-faring man, and never has any attacks while at sea. If attacks develop when ashore, they disappear promptly on going out on the sea. After staying 20 minutes in a stable conjunctival and nasal irritation developed with difficult breathing and râles over the lungs. No skin reaction with horse serum but redness and flow of tears came on soon after touching the eye with a finger that had touched a horse shortly before. In this case anaphylactic shock developed in a guinea-pig injected with horse serum 48 hours after having been injected with 5 c c of the patient's serum.

5. A woman, aged 25, commenced to suffer from asthma when 16 years old, without any warning, and without ever before having felt any peculiar symptoms when in contact with horses. The attacks grew worse, and 4 years later when in a riding school a very severe asthmatic state developed and blisters came out all over the face. This repeated itself after new attempts to take riding lessons. She now was so sensitive that by merely standing next to a person whose clothes had the least bit of horse smell, the eyes would begin to itch and pain and asthma would come on. Once an attack came on after sleeping in a bed covered with an overcoat used in driving. If on returning from driving her husband kisses her, blisters develop in the face and itching of the eyes. Her attacks are brief. She has no hay-fever and there is no history of asthma or hay-fever in the

<sup>2</sup> Jour. Am. Med. Assn., 1905, 52, p. 580.

family. She gives well marked skin reaction to horse serum and the eye reacts promptly when touched with a finger that has come just barely in contact with a horse.

6. A man, aged 42, had asthma since his 10th year, but it was not until his 18th year that he understood that the asthma was connected in some way with horses. A stay of 5 minutes at the side of a horse was sufficient to bring on an attack, but attacks come on which cannot be traced to horses, especially in cold damp weather. The attacks are associated with pain in the abdomen and vomiting. No hay-fever; no asthma or hay-fever in the family. Both lungs are emphysematous, the chest barrel shaped. Horse serum does not cause any skin reaction, but eye reaction to the finger test is prompt.

7. A man, aged 22, has had asthma since his 10th year, dampness, dust, and cold weather apparently bringing on the attacks. When 18 years old, however, he noticed that close association with horses, cattle, and wet dogs would cause attacks. He has hay-fever, and his father has bronchial asthma. Horse serum does not cause any skin reaction, but touching the eye with a finger which has just been in contact with a horse is followed in 5 minutes by itching, redness, tears, but no sneezing.

8. A man, aged 35, would get itching of the eyes, lachrimation, sneezing and coughing with dyspnea whenever in contact with horses. This has been the case since his 5th year. Eating strawberries, either fresh or as jam, would be followed by pressure in the chest and dyspnea. He is a sea captain, and never has asthma when on the sea. The skin reaction with horse serum could not be obtained, but the eye reacted promptly to the finger test.

In addition to these cases, in which the asthma was known to be precipitated by contact with horses, I have studied also a number of asthmatic patients, persons who could not trace their attacks to association with horses or other animals.

9. A woman, aged 34, has had asthma as long as she can remember; as she did not associate her attacks with anything in particular, I asked her to stay in a stable for awhile. After 10 minutes she came out with red, overflowing eyes, nasal discharge, and asthmatic breathing—recovery in 5-6 hours. The eye and skin tests gave only mild reactions. Subsequently I learned that she was very much better so long as she kept away altogether from horses.

10. A man, aged 23, with asthma since childhood, stated that the attacks often came on some 2-3 hours after meals especially after supper. His diet was changed so that he had no bread for breakfast and supper, only mush and milk. On this diet for 3 months he had no attacks, but soon after commencing to eat bread again the asthma reappeared; on restricting him to hard bread only the asthma grew better again. Contact with horses had no influence. No eye or skin reactions.

11. A man, aged 27, began to have asthma when 23 years old; the attacks usually came on at night and would continue for about 2 weeks. He would be well for long periods, no reason being apparent for the asthma which was not in any way connected with horses. The mattress and pillow on which he slept were filled with horse, cow, and cat hair besides wool and were not very clean; on changing to mattress and pillow filled with vegetable matter great improvement took place. He gave an eye reaction by touching the eye with a finger

which had stroked a cat. Holding a cat for half an hour caused the patient to feel badly and to have mild asthma. He does not have hay-fever, but members of his family have hay-fever and asthma.

I have examined 18 cases of ordinary bronchial asthma without being able to discover any relation to horses or to find any exciting cause.

Of the 9 cases described in which the asthma seemed to be dependent in some way on horses, four (Cases 1, 2, 3, and 5) gave a positive skin reaction to horse serum. By scratching the skin and then placing a little horse serum on the scratch, a red spot would appear in from 2 to 10 minutes and persist for an hour or so. All the cases gave eye reaction, that is, touching the conjunctiva with a finger which had just touched a horse would cause a redness to appear in a few minutes with itching, sometimes edema and sneezing, with increased secretion.

As it naturally would be advisable to apply some test in the case of persons suspected of being sensitive to horse emanations, before injecting horse serum, I have made the eye and skin reactions with horse serum on 30 students, all negative; on 12 hay-fever patients, all negative both in and out of the hay-fever season; and as mentioned, on 18 patients with bronchial asthma, also all negative. This result indicates that a positive skin or eye test with horse serum points very definitely to the existence of sensitiveness to horse proteins.

The question now arises, Is it safe to inject asthmatics who give negative skin and eye reactions with horse serum? Gillette and others warn against injecting all asthmatics. I know of 6 hay-fever patients who have been injected with horse serum without any ill effects, and also of 3 asthmatics. Hence it would seem to be quite safe to inject hay-fever and asthma patients who are not sensitive to horse emanations, but in the case of such as are sensitive the injection is unquestionably very dangerous. For this reason all asthmatics and hay-fever sufferers should be tested with the eye reaction and the skin reaction before horse serum is injected, as they may not be aware that their condition stands in any relation to horses.

The question arises whether persons previously injected with horse serum would give any skin or eye reaction. It has been found by Dr. Schönfelder that of 15 such persons not a single one gave a reaction. Of course this does not mean that reinjection of horse serum in such a person never will give rise to any severe symptoms; on the other hand, it is probably the case that in a person once injected with horse serum, who gives a skin or eye reaction, a reinjection very likely would cause

severe symptoms. In this connection a case described by Walker<sup>3</sup> is of great interest: A woman, aged 20, who had not had asthma before, received an injection of horse serum without ill effect; 2 weeks later she began to have attacks of asthma whenever she came into close contact with horses; alcoholic extract of horse dandruff gave a skin reaction. This case suggests that if a large number of skin and eye tests were made soon after injection of horse serum a few reactors would undoubtedly be found.

I have had occasion also to make some observations on somewhat different forms of sensitiveness.

12. A man, aged 30, was always unable to play with cats without irritation of the eyes; occasionally blisters of the skin would develop also. He has no asthma and there is no asthma or hay-fever in the family. The mere presence of a cat would not affect him, but if a finger which had just touched a cat was placed on the conjunctiva tears would begin to flow and there would be itching



Fig. 1.—Lacrimation, itching and redness of the eyes with gradual chemosis and edema of the tissues; the effect of contact of the finger which had just touched a cat on the conjunctiva.

and redness of the eye, and gradually chemosis and edema of the tissues at the inner angle would develop (Fig. 1). These changes would disappear in about 3 hours. If the hair of a cat gets into the eye the same changes occur, and if a cat scratches the skin a large blister forms. Five c c of blood were injected into a guinea-pig; 48 hours later cat serum was injected and there resulted an immediate anaphylactic shock with death. No further experiments were permitted by the patient.

13. A man, aged 36, has had hay-fever in mild degree since puberty; there are 2 cases of hay-fever in the family. He is not sensitive to horses and gives no reaction, either eye or skin; he once received an injection of diphtheria serum without any ill effects. For many years he has had diarrhea with colic in the summer-time, without any known cause except that these disturbances were closely connected with the attacks of hay-fever. If he went into the mountains in the summer both the hay-fever and the diarrhea would disappear.

14. A man, aged 32, noticed since early childhood that when among flowers he would sneeze and itch in the eyes; the smell of flowers especially of roses had the same effect. Whenever exposed to such odors for 15-20 minutes, colic

<sup>3</sup> Jour. Med. Research, 1917, 36, p. 427.

and diarrhea come on, sometimes to his great embarrassment. Whenever he goes to a party he remains as far away from the floral decorations as possible. While under my observation, he kept his nose for 15 minutes in a bunch of roses with the result that diarrhea came on. Scratching the skin and then putting some rose juice on the scratch resulted in an insignificant swelling.

Some of the patients whose asthma was connected with horses seemed to be sensitive only to horses, while others were influenced also by climate and other conditions. In some cases the patients themselves were not aware of their sensitiveness to horses, but ascribed their illness to dampness, etc. Some of them also suffered from hay-fever (Cases 7 and 8); in a few cases other animals seemed to influence the asthma. In some instances the patients could recall that horses made them feel badly ever since their earliest days; others had noticed it since their 10th year or so; others again since their 16th or 18th year.

It is quite impossible to determine whether this sensitiveness is acquired or inborn. It would seem likely that in some cases at least the condition is inborn, but we know that it may be acquired as shown by the woman whose asthma developed after the injection of horse serum (Walker). It is possible that eating horse meat for a long time also may have an influence. The occurrence of "horse asthma" in more than one member of the same family has not been noticed, but families in which bronchial asthma and hay-fever occur seem to be especially predisposed. It is noteworthy that sometimes there are intestinal disturbances associated with the asthma. Attacks of vomiting and pain in the abdomen may occur at the same time as the asthmatic attacks or independently. In Walker's 40 cases of asthma, 3 or 4 presented such symptoms. It is of interest to note here that vomiting may occur in the typical anaphylactic shock. Diarrhea may also develop in connection with the asthma; in one patient diarrhea and hay-fever were associated, coming on and disappearing together. Here may be mentioned again the case of sensitiveness to roses, in which sudden attacks of diarrhea would come on. In anaphylactic shock there often is congestion, hemorrhages, and excessive formation of mucus (enteritis anaphylactica), and Schultz<sup>4</sup> observed that a piece of intestine in Ringer's fluid would contract if horse serum was added to the fluid and that the contraction was far stronger if the intestine came from a sensitized animal, indicating that the antigen uniting with the antibodies in the tissues greatly increase the muscular contractions.

<sup>4</sup> Jour. Pharmacol. and Exper. Therapeutics, 1910, 1, p. 549.

What sort of substances are the patients in question sensitive to? Most likely some form of protein as illustrated by the sensitiveness to pollen in hay-fever. We know that in some cases as in my Case 1 and the cases described by Willey, Gillette, Bacon and Wright, typical shock may follow injection of horse serum in persons sensitive to horses and that there may supervene a state of antianaphylaxis which may last for 3 or 4 months; furthermore that, as in Cases 1, 4, and 12, sensitiveness to horse serum may be transferred to guinea-pigs with the serum of the patients, which constitutes a perfect analogy to passive anaphylaxis. All these facts point to a state of sensitiveness to foreign protein, which may be contained in the sweat and dandruff of the animals concerned. That such must be the case is indicated by the skin and eye reactions which I have described. But it is hard to explain how the patients are influenced when attacks develop without being in close contact with the animals. It seems as if a diffusible substance was in the air. Another difficult question is, How do the antibodies, which are regarded as éssential for the reactions of hypersensitiveness develop in these individuals? Here we are reduced to conjecture and it lies near at hand to assume the existence of some anomaly of protein assimilation. Be that as it may, the conception that these forms of asthma are expressions of hypersensitiveness gives us a basis for rational treatment, namely, by exclusion of the substances concerned, the antigens, on the one hand, or by a gradual immunization with the antigens on the other hand, in order to bind the antibodies without causing noticeable symptoms, as adopted recently with promising results by Walker.<sup>3</sup>